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			EXAMINER LI, BAO Q	
			ART UNIT 1648	PAPER NUMBER

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Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

**Application No.**

09/734,221

**Applicant(s)**

LITTMAN ET AL.

**Examiner**

Bao Qun Li

**Art Unit**

1648

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 29 September 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-26,33-40 and 61-73 is/are pending in the application.
- 4a) Of the above claim(s) 1-26,33-36,38-40,61-69,72 and 73 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 37 and 70 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date 12/11/2000.
- 4) ☒ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. 12/13/2004.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☒ Other: sequence letter.

### **DETAILED ACTION**

The preliminary amendment filed on December 11, 2000 has been noticed. Claim 27-32 and 41-60 have been canceled. Claim 37 has been amended. New claims 70-73 have been added. Claims 1-26, 33-40 and 61-73 are pending.

#### ***Election/Restrictions***

1. Applicant's election with traverse of Group X, claims 37 and 70 in the reply filed on 08/25/2004 is acknowledged. The traversal is on the ground(s) that applicants assuming that search and examination of the entire Application can be made without serious burden, even though it includes claims directed to distinct or independent inventions. Because the commonality of the claims in groups I-III, and V with elected group X all are all related to the mechanism by which HIV entry/translocation into a host cell is enhanced by the presence of the translocation agent CCR5 in the cell and cause the disease. Applicants further submit that the Groups designated by the Examiner fail to define compositions and methods with properties so distinct as to warrant separate Examination and Search.
2. Applicants' argument has been fully considered. However, it is not found persuasive. Because while different inventions are somewhat related to CCR5, they are filed as each of independent and patently distinct inventions. Moreover, the different inventions are disclosed of not using together, and have different modes of operation that previous Office Action has already explained and will be further explained in detail in this office set forth below:
3. For example, the elected group X and group I are patentable distinct in that the group X, claims 37 and 70 are drawn to an in vitro cell line assay for selecting a therapeutic agent for blocking CCR5 mediated a macrophage tropic (M-tropic) HIV-1 envelope protein mediated fusion. The search is related to a CCR5/M-tropic envelope protein mediated fusion or M-tropic HIV-1 infection at the early step of virus fusion. In contrast, the invention of group I, claims 1-6, is directed to a method for identifying a presence of a translocation-promoting agent on a cell surface (including CCR5 or CXCR4 or CCR2 or CCR3 etc). First, it is not related to selecting a CCR5 inhibitor, it is rather related to identifying the translocator, such as CCR5 expression on cell surface. Secondly, the translocation-promoting agent is not limited to CCR5. Furthermore, the search does not related to any thing about an inhibition of M-tropic HIV-1 virus mediated

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fusion or infection. The assay for identifying receptor presence is just a receptor binding assay rather than a virus fusion assay or M-tropic HIV-1 virus infection. Apparently, the search for group X differs from that of group I, and are not coextensive.

4. Group X and Group II are patentable distinct. Group II of invention is drawn to a method for identifying viral envelope glycoprotein binding to a translocating promoter agent in a solid phage assay, and it is not a living cell based fusion assay. It has is patentably distinct and has different state of art and searching. Furthermore, the assay for identifying the binding site of envelope protein to the receptor CCR5 may have noting to do with screening an inhibitor against M-tropic HIV envelope fusion or infection. Apparently, group II and Group X require different searches.

5. The elected group X is patentable distinct from group III, claim 10, because claim 10 is directed to a method of identifying a drug modulating an expression of a cell receptor CCR5 or CXCR5 etc. First, the scope of the group III is not limited to the agent can inhibit the translocator CCR5, it is directed to any agent that can modulate (increase or suppress) the expression of any translocation promoting agent including CD4, CXCR4, CCR5, and CCR3 etc. Moreover, the method is not related to the screening assay using a HIV-1 M-tropic envelope protein mediated fusion or M-tropic HIV-1 infection. Therefore, it require different search and has different state of art. For example, cytokine GM-CSF can modulate the CCR5 expression on peripheral blood mononuclear cells (PBMC), it does not inhibit the HIV-1 M-tropic envelope protein mediated fusion, or M-tropic HIV-1 infection. Quit oppositely, it enhances the M-tropic HIV-1 infection as

6. The elected group of X is patentable distinct from allergy group V, claims 14-18, because the group V is directed to an in vivo treatment of a mammal in vivo with a fusion inhibitor, which is not related to an in vitro cell line screening assay. Therefore, they have different state of art and require different searches.

7. The requirement is still deemed proper and is therefore made FINAL.

8. Claims 37 and 70 are considered before the examiner.

#### *Sequence requirements*

9. This application contains sequence disclosures **in lines 24-25 on page 16** that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37

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CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

10. Full compliance with the sequence rules is required in response to this Office Action. A complete response to this office action should include both compliance with the sequence rules and a response to the Office Action set forth below. Failure to fully comply with **both** these requirements in the time period set forth in this office action will be held non-responsive.

### *Specification*

11. The 'Brief Description of the Drawings' for Fig. 3 on page 15 of the specification is objected to. While the actual drawings identify the Figure as Figures 3A to 3J, the 'Brief Description of the Drawings' on page 15 of the specification refers to the figure as Figures 3a-3d. Amendment to page 15 of the specification is suggested to reflect this. References to the Figure throughout the specification should be amended accordingly.

### *Claim Rejections - 35 USC § 112*

12. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

13. Claims 37 and 70 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for having a method of screening an HIV-1 macrophage tropic (HIV M-tropic) fusion inhibitor with cells expressing both CD4 and CCR5 in the presence of M-tropic HIV-1 infection or a virus pseudotyped with a full-length of HIV M-tropic envelope protein, wherein the inhibitor can be used for treating a patient infected with a M-tropic HIV virus sensitive to the said inhibitor, does not reasonably provide enablement for a method of screening any or all HIV fusion inhibitor with a cell that only expresses CCR5 in the presence of any or all kinds of HIV isolates or any or all kinds of viruses pseudotyped with any or all kind of

M-tropic envelope, wherein an inhibitor identified by the method can be used for prevention of AIDS. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

14. The test of scope of the enablement is whether one skilled in the art could make and use the claimed invention from the disclosure in the application coupled with information known in the art without undue experimentation (See *United States v. Theketrone Inc.*, 8USPQ2d 1217 (Fed. Cir. 1988). Whether undue experimentation is required is not based upon a single factor but rather a conclusion reached by weighting 7 factors. These factors were outlined in *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and again in *re Wands*, 8USPQ2d 1400 (Fed. Cir. 1988). The scope of enablement issue is analyzed according to these factor set forth below:

15. (1) & (2) State of art and unpredictability.

16. It is well known in the art that family of HIV-1 has tropisms. The T-cell tropic HIV-1 virus only infects T-cells that express HIV-1 receptor CD4 and its fusion co-factor of  $\alpha$ -chemokine (or CXCR4 chemokine) receptor, CXCR4. The M-tropic HIV-1 only infects macrophage or monocyte that express HIV-1 receptor CD4 and its fusion co-factor of  $\beta$ -chemokine (or CC-chemokine), CCR5 (Broder et al. *Pathology* 1996, Vol. 64, No. 4, pp. 171-179, see entire document). The Dual tropic primary HIV-1 isolate infects its target cell by using either the  $\beta$ -chemokine receptor CCR5 (synonym as CKR-5), CCR3 (synonym as CKR-5) or CCR2b (synonym as CKR-2b) (Doranz et al. *Cell* 1996, Vol. 85, pp. 1149-1158). Hence, different HIV-1 viruses use different chemokine receptors as their fusion cofactor in conjunction with an HIV-1 binding receptor CD4 to fuse and infect with the host cells. Therefore, it is unpredictable for testing a R5 HIV-1 fusion inhibitor with a cell that only expresses CCR5 without CD4.

17. This unpredictability is also demonstrated by applicants' own work published on *Nature* (Deng et al. *Nature* 1996, Vol. 381, pp. 661-666, Fig 2c on page 663) and disclosure in specification (See line 27 on page 1 and lines 15-18 on page 51 and lines 25-29 on page 48, lines 15-17 on page 51, Fig. 2C, Fig. 3A, Fig. 3I). Both Deng's publication and specification teach that chemokine receptor CCR5 and receptor CD4 cooperatively mediated entry of M-Tropic (See

examples 1-4) The M-tropic HIV-1 can not infect the cell line that only the chemokine receptor CC-CRK5 (synonym of CCR5) or fusin (synonym of CXCR4). The assay for testing inhibitory effect against HIV-1 M-Tropic envelope mediated fusion can also be processed on the cell line that expresses both CD4/CCR5. If the test line only expresses CC-CKR5 (CCR5) without CD4, it fails to support the virus entry. Applicants do not teach that a cell line with only CCR5 (CC-CKR5) expression can be infected via T-tropic HIV-1 envelope mediated fusion. Actually, applicants teach that the 3T3 cell with CD4 and CC-CKR5 expression cannot be infected with T-tropic HIV (HXB2 strain) (Fig. 3A).

18. Moreover, state of art also teach that the susceptibility of monocytic THP-1 cell line to R5 (M-tropic, such as HIV-1<sub>Bal</sub>) or X4 (T-tropic, such as HIV-1<sub>IIIB</sub>) HIV-1 isolate infection depend on expression of CD4 rather than CCR5 or CXCR4 on the cell surface as evidenced by Konopka et al. (AIDS RESEARCH AND HUMAN RETROVIRUSES 2002, Vol. 18, No. 2, pp. 123-131, see entire document, especially abstract, page 125, 3<sup>rd</sup> paragraph, Fig. 1 on page 127).

19. Furthermore, not all M-tropic envelope mediated fusion uses CCR5. For example, Igarashi et al. disclose that a chimeric M-tropic envelope of simian/Human Immunodeficiency uses CXCR4 not CCR5 to mediate fusion as evidenced by Igarashi et al. (Journal of Virol. 2003, Vol. 13042-13052, see page 13042, and line 11-13 on the 1<sup>st</sup> col. of page 13050, and Fig. 6 on page 13048). Therefore, it is unpredictable for using a virus pseudotyped with any or all kinds of macrophage-tropic envelope protein to do the R5 mediated fusion inhibitor screening assay.

20. Regarding to the limitation of selected agent that can be used for preventing AIDS, the claim 6 is drafted as a reach-through claim and this also is rejected because the claim does not comply with the "how to make" prong of the enablement requirement for the reasons analyzed by weighting 7 factors outlined in Ex parte Forman, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and again in re Wands, 8USPQ2d 1400 (Fed. Cir. 1988) set forth bellow:

21. The state of art teaches that fusion inhibitor such as T20 (enfuvirtide, ENF) can be used for inhibiting HIV-1 envelope protein mediated fusion. However, HIV-1 virus develop a resistance in response to a fusion inhibitor treatment. Therefore, it is unpredictable for using the inhibitor for preventing AIDS. For example, the amino acid mutations in positions from 32 to 45 of HIV-1 envelope transmembrane domain gp41 change the susceptibility of virus to the T20 treatment in vitro and in vivo as evidenced by Wei et al. (Antimicrobial agents and

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chemotherapy 2002, Vol. 46, No. 6, pp. 1896-1905, see entire document, especially page 1896, Figs. 2-6), Sista et al. (AIDS 2004, Vol. 18 (13), pp. 1787-1794, See pages 1790-1794) and Greenberg et al. (J. Antimicrobiol Chemotherapy 2004, Vol. 54, pp. 330-340, Table 1 and page 336-337).

22. (3) & (4) Working example and adequate guidance.

23. The specification only teaches to use a cell line that expresses both CD4 and CCR5 infected with M-tropic HIV-1 virus or virus pseudotyped with the full-length M-tropic HIV-1 virus for doing the screening assay, and the inhibitor identified by the method e.g. RANTES or MIP-1 $\beta$  will block the M-tropic HIV-1 envelope protein mediated fusion and inhibit the M-tropic HIV-1 infection. The specification lacks of teaching any M-tropic HIV-1 fusion inhibitor that can be used for preventing AIDS.

24. (5)-(7) The scope of claims, nature of invention and level skill in the art:

25. The scope of claims are broadly read on the method for identifying an agent that can be used for treatment or prevention of AIDS comprises to use all cell as long as it express CCR5 in any or all HIV infection or any virus pseudotyped with any or all M-tropic envelope protein. The nature of invention is an assay for screening an agent that can be used for treating or preventing AIDS. Therefore, the skill in the art to perform the full scope of the claims are quit high, especially in view of the unpredictability as described supra.

26. Given the above analysis of the factors, it is concluded that the skilled artisan would have conducted undue and excessive experimentation in order to practice the claimed invention.

### ***Double Patenting***

27. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

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28. Claim 37 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 13-20 of U.S. Patent No. 6,258,527B1. Although the conflicting claims are not identical, they are not patentably distinct from each other because method steps cited in claims 13-20 in patent "527" comprises all steps claim 37 drafted. For example, claim 37 is drawn to a screening assay comprising contacting an agent with a cell expressing CCR5 on the cell surface with an HIV virus or a virus pseudotyped with a M-tropic envelope protein, and measuring the fusion between the virus and the target cell. The method of claims 13-20 is to identify a drug or an antibody that interferes with the translocation of HIV-1 into the transformed cell via the translocation promoter agent (which is CC-CKR5 or CCR5) by measuring the inhibition of envelope protein mediated and a reporter gene involved fusion assay. The assay comprises administering an agent or antibody to a cell that expresses the chemokine receptor CC-CKR5 (CCR5) in the presence of a primary HIV-1 isolate infection, and detecting if the reporter gene expression is less detectable in the presence of the drug or antibody. In this context, the drug or antibody is the agent; the cell expression CC-CKR5 is the same target cell that expresses CCR5. The primary HIV-1 isolate is the HIV virus. Therefore, claims 13-30 of Patent "527B1" anticipate the rejected claim 37.

***Claim Rejections - 35 USC § 102***

29. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

30. Claim 37 is rejected under 35 U.S.C. 102(a) as being anticipated by Cocchi et al. (Science 1995, Vol. 270, pp. 1811-1815) in light of Moriuchi et al. (J. Immunol. 1997, Vol. 159, pp. 5441-5449).

31. The claimed method is directed to a method for identifying an agent whether or not it can influence the HIV-1, preferably M-tropic HIV-1 envelope fusion or entry into a target cell, said method comprise contacting an agent with a cell having a CCR5 expressing on the cell surface in the presence of an HIV virus or a virus psuedotyped with an HIV macrophage-envelope, and

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measuring whether the agent can inhibit the virus fused with the target cell significantly or the cell get a resistance to the virus fusion or entry. If the inhibition is statically greater enough, the agent is selected.

32. Cocchi et al. teach a method for inhibiting HIV-1 infection comprises contacting the agent of recombinant human C-C-chemokine selected from group consisting of recombinant human RANTES (rhRANTES) or MIP-1 $\alpha$  (rh MIP-1 $\alpha$ ), or MIP-1 $\beta$  (rh MIP-1 $\beta$ ) or MCP-1 with MP1 cell line in the presence of M-tropic HIV-1, such as HIV-1<sub>Bal</sub> or T-tropic HIV-1 virus, such as HIV-1<sub>IIIB</sub> infection, wherein the MP1 cell inherently expresses CCR5 in light of the disclosure of Moriuchi et al. (See the first 2 lines of the 1<sup>st</sup> paragraph of Results on page 5443, 1st column), and the M-tropic HIV-1 inherently comprises the macrophage-tropic envelope. They demonstrate that chemokine rhRANTES, rhMIP-1 $\alpha$  and rhMIP- $\beta$ , but not MCP-1 significantly inhibits the M-tropic HIV-1<sub>Bal</sub> infection. However, they do not inhibit the T-tropic HIV-1<sub>IIIB</sub> viral antigen expression (Figs. 3 & 4 on page 1814). While the assay shown by Cocchi et al. is not a fusion assay, the result of the decreased M-tropic virus infection inherently is the cause of the fusion inhibition by the chemokine rhRANTES or rhMIP-1 $\alpha$ , rhMIP- $\beta$ 1. To this extent, it can be considered as one of the data reflecting the result of inhibiting M-tropic HIV1 envelope protein mediated fusion. Nevertheless, the assay disclosed by Cocchi et al. teach each of the limitations as claim 37 drafted. Therefore, the cited reference inherently anticipates claim 37.

33. Regard to this prior art inherency anticipatory rejection, Applicants' attention is directed to Feit et al. (2003, J. Pat. Trade. Off. Soc., Vol. 85, No. 1, pages 5-21). In that article, Feit et al. teach three criteria for inherency. (1) The most important criterion is certainty. Citing *In re Tomlinson* and *In re Zierden*, Feit et al. state that certainty is established when the reference process necessarily **results** in the claimed process as opposed to a **possibility**. (2) The second criterion is chronology; it will always happen. Feit et al. state that the chronological test is forward chronology. Citing *Eli Lilly and Co. v Barr Laboratories, Inc.*, Feit et al. argue that the claimed result must always be obtained based upon the prior art method. 3) The third criterion is the legal standard. Feit et al., citing *Continental Can*, state that the legal standard is whether the missing descriptive material would be so recognized by a person of ordinary skill in the art as necessarily present in the thing. Feit et al. further emphasized that determination about whether

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the claimed element is inherent in the prior art is the objective understanding of a person having ordinary skill. If the person having ordinary skill presented with the facts would understand that the prior art inherently disclose a claimed element, the element is anticipated. It is irrelevant whether the understanding was apparently at the time of filling the application in question (As in continental Can, Robertson and Telemac), or first becomes apparent at a later time (as in Atlas Powder and MEHL/Biophile).

34. In the instant case, while the mechanism of inhibition of HIV-1 M-tropic virus infection by C-C chemokine, rhRANTES or rhMIP-1 $\alpha$ , rhMIP-1 $\beta$  is certain because it is later recognized by the person skill in the art that CCR5 is a fusion co-factor for M-tropic HIV-1 envelope protein mediated fusion. The C-C chemokine: RANTES or MIP-1 $\alpha$  or MIP-1 $\beta$  is the CCR5 native ligand, which binds the CCR5 with much higher affinity. Therefore, the effect of using CCR5 ligand of C-C chemokine treatment to inhibit the M-tropic HIV-1 virus fusion and infection via blocking the fusion co-factor CCR5 will always happen and be accepted by the person skill in the art. Even though the fact was later recognized by person skill in the art post filling date of the current application, according to Feit et al. it is irrelevant whether the understanding was apparently at the time of filling the application in question.

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The claim 70 is free of prior art rejection because prior to the current application was filed, no prior art teaches or suggests that screening the HIV-1 M-tropic envelope protein mediated fusion, the method should include the step of testing if the agent binds to CCR5 because the logical connect between the CCR5 and M-tropic HIV-envelope is recognized post filling date of current application which the most closest art by Cocchi et al. has taught the CC-chemokine RANTES or MIP- $\beta$ 1 inhibit the HIV-1 infection, in which the assay used by them include all limitations of claim37, they did not teach or suggest that the method for identify the inhibitor include or should include the step of testing the candidate agent binding to CCR5.

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***Conclusion***

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bao Qun Li whose telephone number is 571-272-0904. The examiner can normally be reached on 7:00 am to 3:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Bao Qun Li, M. D.

12/13/2004